REMARKS

Claims 5-8 are being examined and have been rejected. Claims 9-24, 28-30, 32-34, 36, 56-58, 62, 67-72, 75-76, and 79-83 are drawn to a nonelected subject matter and have been withdrawn. Applicants respectfully note that claim 25 is also drawn to a nonelected subject matter, and thus is withdrawn from further consideration.

Claim Objections

Claims 5 and 8 were objected to for reference to table 1 and because they encompass non-elected subject matter (i.e., sequences other than 107).

In response, claim 5 has been amended to recite the HSP150 gene while claim 8 has been amended to recite SEQ ID NO: 107 (the elected sequence).

Rejection Under 35 U.S.C. 112

Claims 5-8 were rejected under 35 U.S.C. 112, paragraph 1, as allegedly failing to meet the enablement requirement. The rejection argues several points:

1. Nature of the Invention

The rejection is based on the interpretation that the claim is drawn to a method of diagnosing cancer based on measuring elevated copy number of the HSPC150 gene, the cDNA sequence for which is provided as SEQ ID NO: 107. The argument is based at least in part on the concept that this is an "unpredictable art" as supported by the case of *Mycogen Plant Sci. v. Monsanto Co.*, 58 USPQ2d 1030, 1041 (Fed. Cir. 2001).

In response, Applicants respectfully disagree and assert that they have made the art predictable by providing the sequence to be measured and the phenotype (i.e., increased copy number) to be determined. The Examiner's quotation from *Mycogen* is from a portion of the opinion relating to conception and reduction to practice where both litigants were trying to establish priority. In the present case, Applicants' filing of the application is a constructive reduction to practice and Applicants teach all that is necessary to carry out the claimed method.

Further, the present invention is a diagnostic procedure. Applicants teach that the subject gene (HSCP150) is related to breast cancer (see page 28, line 17, of the application as-filed, where breast cancer is linked to the first 229 genes). Further, Table 1, at gene No. 119 (SEQ ID NO: 107) clearly teaches that this gene is related to breast cancer metastasis (columns 4 and 5 of the table).

In this regard, Applicants respectfully direct the Examiner's attention to the "Patent Examination Policy - MPEP Staff - 35 USC 112 1st para - Enablement of Chemical/Biotechnical Applications. TRAINING MATERIALS FOR EXAMINING PATENT APPLICATIONS WITH RESPECT TO 35 U.S.C. SECTION 112, FIRST PARAGRAPH-ENABLEMENT OF CHEMICAL/BIOTECHNICAL APPLICATIONS (1996)" (obtained from the PTO Website) wherein it is stated for diagnostic assays:

> **III. (A) (2) (b) (ii) (b) Diagnosis Assays**
>
> Unless a specification specifically states something to the contrary, the term "diagnostic assay" is to be construed to mean any assay that can be used to help diagnose a condition, as opposed to an assay that can, in and of itself, diagnose a condition. A diagnosis is typically made by evaluating the results of several screening assays, each of which has some level of false results and, accordingly, each of the screening assays would be a "diagnostic assay". Therefore, **to enable a diagnostic assay use, a disclosure merely needs to teach how to make and use the assay for screening purposes**. [Emphasis added]

Applicants respectfully contend that they have met this requirement. Thus, Applicants teach a specific sequence (SEQ ID NO: 107) that represents the cDNA for a stated gene, provide a determining factor for measure (i.e., copy number), means for determining this quantity (copy number analysis is well known in the literature, the means by which the candidate gene was identified (application at page 9, lines 21-24) and positive steps in the assay procedure (as set out in claim 5). In sum, Applicants have done as much as is required.

2. Scope of the claims

The rejection asserts that claim 5 is drawn to use of any mammal and any type of cancer. While that is true, the steps of the assay are clearly recited and are limited to measuring copy number of a stated gene. The identity of the mammal to be diagnosed and/or the cancer to be detected is not relevant to practicing the claimed method and is in no way limiting. The nature of a diagnosis is "to find out" and thus knowing the mammal and/or the tissue to be tested is not essential to the claimed method. If it were, one would know the answer to the question before they perform the diagnostic method of the claims.

As noted in the quoted guideline above, a diagnostic assay merely helps to diagnose, is only part of an overall procedure and each such procedure is subject to some level of false results. In short, if the clinician wanted to know whether a cancer is malignant or not, he would first have to know there is a cancer. However, the present diagnostic is to determine the possibility of cancer so that the presence of a cancerous condition is not known beforehand. Thus, conceivably, any mammal could be tested using the diagnostic procedure of the invention and any tissue of said mammal, including a human, could be tested simply because, until such testing, the clinician or veterinarian has no idea if cancer is present or not (except by the outcome of other ancillary tests).

3. Teachings in the Specification and Examples

The rejection contends that Table 1 fails to identify whether the over-expression is based on copy number or not. Applicants respectfully disagree and note that Table 1 is a list of genes identified in cancerous cells as being both over-expressed and showing increased copy number. The procedure for generating the list of genes found in Table 1 is summarized on pages 7-10 of the specification as-filed. Therefore, the specification provides adequate support for the HSPC150 gene having an increased copy number in cancer or pre-cancerous conditions. Applicants remind that they merely need to teach how to make and use the invention in order to meet the enablement requirement (see above).

4. State of the Art and Unpredictability of the Art

The rejection cites varied ways to increase expression without increasing copy number. However, nowhere is it shown that increased copy number is not related to metastasis, as is taught by Applicants. Instead, several research papers are referred to, which speculate on the relationship between increased copy number and cancer. The problem with this lime of argument is that none of the papers relate to the gene recited by Applicants.

As previously stated, Applicants note that Table 1 is a list of genes identified in cancerous cells as being both over-expressed and showing increased copy number. Therefore, the HSPC150 gene was found to have an increase in copy number and was overexpressed.

Additionally, Applicants submit the attached paper by Lemaire et al. (Brit. J. of Cancer, Vol. 89, pp. 1949-1949 (2003)), published just prior to Applicants' international filing date but after Applicant's priority date. Lemaire et al. show (see page 1945, col. 2, last line, over to page 1946, col. 1, and in Figure 6A) that HSPC150 is over-expressed in human head and neck tumors.

The rejection also contends that it is unpredictable as to whether the method of the claims could be extrapolated from humans to other mammals. In response, Applicants respectfully remind that other mammals are often successfully used a models for cancer in humans and that Applicants' claimed method provides a means of making just such a determination.

5. Quantity of Experimentation

The Examiner alleges that there is "no evidence in the specification that increased copy number of HSPC150 is actually associated with cancer or pre-cancerous conditions", thereby necessitating undue experimentation, such as producing probes for this gene to be tested in large numbers of different tissues in large numbers of different mammals.

Applicants respectfully disagree and point out that on pages 7-10 of the specification as-filed, Applicants have described the procedure used to identify genes including HSPC150 that have increased copy number in cancer or pre-cancerous conditions.

Furthermore, Applicants assert that no undue experimentation is necessary.. Applicants have enabled the skilled artisan to practice the claimed invention by listing methods known in the art, for example, on pages 26-28 of the specification as-filed. The Examiner is not describing experimentation, which is drawn to developing an assay. Instead, Applicants' claims are drawn to using an assay, for which Applicants have provided a specific gene (HSPC150), a specific sequence (SEQ ID NO: 107), a

parameter to be measured (gene copy number) and positive steps for measurement (comparing the test sample with normal tissue).

Having the sequence means that it is a minor detail to synthesize probes (which may already exist because this gene is well known in the art). Testing different tissue samples from different mammals does not involve undue experimentation because it is well known how to measure copy number. Applicants respectfully remind the Examiner that the claims are drawn to a diagnostic procedure and not to a means for developing such a procedure or to a method of studying a cancer already known to be present. In fact, the Examiner's characterization of "undue experimentation'" is merely a description of carrying out the steps of the claimed method (which no one can do without doing it).

It is settled law that the mere fact that many analyses must be performed to carry out the claimed method does not *per se* amount to undue experimentation. *In re Wands,* 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), a case involving immunoassays employing monoclonal antibodies for detection of hepatitis B surface antigens. The PTO had found the claim invalid for lack of enablement but the court reversed, holding that the specification was enabling and finding that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening" and that "a considerable amount of experimentation is permissible, if it is merely routine" (citing In re Jackson, 217 USPQ 804, 807 (Bd. App. 1982). The Court's conclusion was that there was "a high level of skill in the art at the time the application was filed" and "all of the methods needed to practice the invention were well known." (8 USPQ2d at 1406) so that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." (8 USPQ2d at 1407)

In the present case, the level of skill in this art is high and, unlike the need to prepare antibodies from scratch (as in Wands), those seeking to use the invention merely need to prepare probes based on the sequence taught by Applicants. In addition, whether there would be the necessity to screen different mammals and/or different tissues is irrelevant because screening is what the claim is about. The claims

are drawn to a screening method for increased copy number of a specific gene or nucleotide sequence and not to a method for finding out if a correlation between copy number and cancer exists or not. All one needs to do to carry out the claimed method is determine the copy number in cells of a tissue sample.

Based on the the foregoing, it is evident that the specification has met the enablement requirement. Accordingly, applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

CONCLUSION

In view of the above recited amendments and remarks, Applicants respectfully request that the Examiner reconsider the patentability of the pending claims.

Applicants believe that no fee is due in filing this response. The Commissioner is requested to charge any additional fees, or credit any refunds, to Deposit Acc't No. 03-0678.

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